UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/055,713	01/22/2002	Andrew Jamieson	8325-0026	6239

23419 7590 10/06/2003

COOLEY GODWARD, LLP
3000 EL CAMINO REAL
5 PALO ALTO SQUARE
PALO ALTO, CA 94306

EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	10

DATE MAILED: 10/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,713	JAMIESON ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group X, filed July 14, 2003, is acknowledged. Upon further consideration the restriction requirement is withdrawn. Claims 1-19 are examined in the instant office action.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, filed December 30, 2002 is attached to the instant Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to isolated polynucleotides encoding plant zinc finger proteins of undefined structure and unknown modification that bind to undefined target sequences of any size and any nature, including such isolated polynucleotides that further encode a domain of undefined structure and function that may repress or activate some unknown

process. The claims are also drawn to isolated polynucleotides encoding modified plant zinc finger proteins comprising a tandem array of any number of any type of canonical or non-canonical zinc fingers, including tandem arrays derived from two or more plant species, wherein one or more amino acid residues of the modified plant zinc finger protein are deleted or substituted as compared to a naturally occurring plant zinc finger protein.

In contrast, the specification describes only a single genus of polynucleotides encoding modified plant zinc finger proteins. The polynucleotides described encode polypeptides comprising a tandem array of three modified canonical zinc fingers, two derived from the *Arabidopsis* zinc finger sequences of SEQ ID NOS: 13 and 14 and one derived from the petunia zinc finger sequence of SEQ ID NO:12, said tandem array being fused to the transcriptional activation domain of the herpes viral protein VP16 (pages 36-42). The zinc finger backbones were modified by amino acid substitution, addition and deletion to more closely resemble the SP-1 consensus sequence of SEQ ID NO:11, resulting in the production of the zinc finger backbones of SEQ ID NOS 17-19. The amino acid sequences of each of the three zinc fingers were further modified to cause the zinc fingers to bind to 16 different specific target sequences in the *Arabidopsis* GMT gene, each target sequence consisting of 10 contiguous nucleotides, and expression of the native GMT gene in *Arabidopsis* protoplasts was enhanced upon expression of the encoded modified plant zinc finger/VP16 fusion proteins relative to expression in transfected control protoplasts (page 42 and Figure 2).

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lily and Co., 119

F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Given the claim breadth and lack of defining features as discussed above, the specification fails to provide an adequate written description of the genus as broadly claimed. Given the lack of written description of the claimed products, any method of using them would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing. See Written Description Requirement guidelines published in Federal Register/ Vol. 66, No.4/ Friday January 5, 2001/Notices: pp. 1099-1111).

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated polynucleotides encoding the exemplified genus of modified plant zinc finger proteins, does not reasonably provide enablement for isolated polynucleotides encoding plant zinc finger proteins of having any and all structural configurations and modifications that bind to target sequences of any size and any nature. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to isolated polynucleotides encoding plant zinc finger proteins of undefined structure and unknown modification that bind to undefined target

sequences of any size and any nature, including such isolated polynucleotides that further encode a domain of undefined structure and function that may repress or activate some unknown process. The claims are also drawn to isolated polynucleotides encoding modified plant zinc finger proteins comprising a tandem array of any number of any type of canonical or non-canonical zinc fingers, including tandem arrays derived from two or more plant species, wherein one or more amino acid residues of the modified plant zinc finger protein are deleted or substituted as compared to a naturally occurring plant zinc finger protein.

In contrast, the specification discloses how to make and use only a single genus of polynucleotides encoding modified plant zinc finger proteins. The polynucleotides disclosed encode polypeptides comprising a tandem array of three modified canonical zinc fingers, two derived from the *Arabidopsis* zinc finger sequences of SEQ ID NOS: 13 and 14 and one derived from the petunia zinc finger sequence of SEQ ID NO:12, said tandem array being fused to the transcriptional activation domain of the herpes viral protein VP16. (pages 36-42). The zinc finger backbones were modified by amino acid substitution, addition and deletion to more closely resemble the SP-1 consensus sequence of SEQ ID NO:11, resulting in the production of the zinc finger backbones of SEQ ID NOS 17-19. The amino acid sequences of each of the three zinc fingers were further modified to cause the zinc fingers to bind to 16 different specific target sequences in the *Arabidopsis* GMT gene, each target sequence consisting of 10 contiguous nucleotides. Expression of the native GMT gene in *Arabidopsis* protoplasts was enhanced upon expression of the encoded modified plant zinc finger/VP16 fusion proteins relative to expression in transfected control protoplasts (page 42 and Figure 2).

While the specification provides guidance for making modified canonical plant zinc finger/ VP16 fusion proteins that transactivate a specific endogenous target gene sequence, the

specification does not provide guidance for making modified non-canonical plant zinc finger proteins. The specification explains a process by which the structure of the zinc finger backbone of canonical plant zinc finger proteins may be altered to more closely conform to the zinc finger backbone of a consensus sequence for a human canonical zinc finger protein SP-1. The specification also indicates that the use of the human canonical zinc finger protein SP-1 in the construction of engineered zinc finger proteins had previously been established in the art, indicating the feasibility of obtaining modified canonical zinc finger proteins based on SP-1 (page 2 line 25 through page 3 line 5). The specification does not, however, explain how to alter the structure of the zinc finger backbone of non-canonical plant zinc finger proteins relative to any established non-canonical zinc finger standard, or indicate the identity of any such non-canonical zinc finger standard. Absent guidance for altering the structure of the zinc finger backbone of non-canonical plant zinc finger proteins relative to an established standard, one skilled in the art would have to resort to trial and error experimentation in order to determine which amino acid residues to add, delete or substitute in the backbone of a non-canonical plant zinc finger protein in order to construct a modified non-canonical plant zinc finger protein that would be functional.

Furthermore, while the specification provides guidance for making modified plant zinc finger fusion proteins that comprise the transcriptional activation domain of the herpes viral protein VP16, the specification does not provide sufficient guidance for making modified plant zinc finger fusion proteins that comprise other types of zinc finger fusion proteins comprising domains known to function in plants. The specification indicates at page 8 the general types of functional domains that could be used in conjunction with modified plant zinc finger proteins, and further indicates specific examples of such potential functional domains at pages 22-24. The

majority of functional domains indicated, however, appear to be mammalian in origin, and their ability to function in conjunction with a modified plant zinc finger protein would be unpredictable. See, for example, Segal et al., teaching that zinc finger fusion protein effector domains that function in one cell type may not function in a different cell type or in a different species due to the specificity of the protein-protein interactions that effect domain function (Curr. Opin. Plant Biol. 2003, Vol. 6, No. 2, pages 163-168, see page 165 column 1 first full paragraph). Absent guidance with respect to the nature and source of functional domains that could be successfully used in conjunction with modified plant zinc finger proteins, one skilled in the art would have to resort to trial and error experimentation in order to identify which functional domains could be used to practice the claimed invention.

Given the claim breadth, and given the lack of guidance for making modified noncanonical plant zinc finger proteins and the unpredictability of heterologous effector domains functioning in conjunction with modified plant zinc finger proteins as discussed above, it would require undue experimentation for one skilled in the art to determine how to make modified noncanonical plant zinc finger proteins and how to use modified plant zinc finger proteins fused with heterologous effector domains.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 12, 14, 15, 16 and 17, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 17 are indefinite in the recitation of "target sequence". It is unclear what type of target sequence the modified zinc finger protein binds. The specification indicates that the target sequence bound by the modified zinc finger proteins exemplified is a DNA sequence, yet the claims encompass any and all types of polymeric target sequences that can be bound by a modified zinc finger protein, including target sequences that that are unrelated to any apparent use of a modified zinc finger protein.

Claim 12 is indefinite in the recitation of "amino acid residues". There is insufficient antecedent basis for the limitation "amino acid residues" in claims 1, 2 and 5 from which claim 12 depends. It is suggested that the claim be amended to indicate that one or more amino acids residues of the protein encoded by the polynucleotide are deleted or substituted.

Claim 14 is indefinite in the recitation of "functional domain". It is unclear what function is performed by the functional domain. The specification indicates that the zinc finger protein DNA-binding domain may be fused to an additional domain that functions to activate or repress transcription from the sequence associated with the zinc finger protein DNA-binding domain target sequence, yet the claim encompasses any polypeptide domain that exhibits any function, including functions that are unrelated to any apparent use of a zinc finger protein DNA-binding domain.

Claim 15 is indefinite in the recitation of "repressive domain". It is unclear what would be repressed by the repressive domain. The specification indicates that the zinc finger protein DNA-binding domain may be fused to an additional domain that functions to repress transcription from the sequence associated with the zinc finger protein DNA-binding domain target sequence, yet the claim encompasses any polypeptide domain would repress any cellular

function, including cellular functions that are unrelated to any apparent use of a zinc finger protein DNA-binding domain.

Claim 16 is indefinite in the recitation of "activation domain". It is unclear what would be activated by the activation domain. The specification indicates that the zinc finger protein DNA-binding domain may be fused to an additional domain that functions to activate transcription from the sequence associated with the zinc finger protein DNA-binding domain target sequence, yet the claim encompasses any polypeptide domain would activate any cellular function, including cellular functions that are unrelated to any apparent use of a zinc finger protein DNA-binding domain.

Claim 17 is indefinite in the recitation of "modified". It is unclear in what way the plant zinc finger protein is modified. The specification at page 18 indicates that a modified plant zinc finger protein is an amino acid sequence, or variant or fragment thereof, which capable of binding to a target sequence and which comprises sequences derived from plant sources which have been reassembled in a non-plant ZFP structure, but it is unclear what would constitute an amino acid sequence "variant", how sequences would be "derived" from plant sources, or what is meant by a "target sequence". Accordingly, the metes of bounds of "modified" in the rejected claim are unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 14 and 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Aoyama et al. (The Plant Journal, 1997, Vol. 11, No. 3, 605-612).

The claims are drawn to an isolated polynucleotide encoding a modified plant zinc finger protein that binds to a DNA target sequence that is 3 or more contiguous nucleotides, and an isolated polynucleotide encoding a modified plant zinc finger protein that further encodes an activation domain. The claims are also drawn to an expression vector and a host cell.

Aoyama et al. teach a tobacco plant host cell and transgenic tobacco plant comprising an isolated polynucleotide encoding a fusion protein comprising the DNA-binding domain of the yeast GAL4 zinc finger transcription factor, the transactivating domain of the herpes viral protein VP16, and the receptor domain of the rat glucocorticoid receptor (page 605 column 2 last paragraph through page 606 column 2 first full paragraph and Figure 1; page 608 Figure 3). The fusion protein taught by Aoyama et al. has the inherent ability to bind to a target DNA sequence that is 3 or more contiguous nucleotides, because the DNA-binding domain of zinc finger transcription factors are known to have this property. The fusion protein taught by Aoyama et al. is also a modified plant zinc finger protein, because it is genetically engineered and because it functions in plant cells.

Claims 1-9 and 12-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Takatsuji et al. (J Biol Chem. 1996 Sep 20; 271(38):23368-73).

The claims are drawn to an isolated polynucleotide encoding a modified plant zinc finger protein comprising a tandem array of canonical C2H2 zinc fingers, one or more of which is obtained by rational design or selection, and said protein having one or more amino acids deleted between one or more of the zinc fingers, wherein said protein binds to a DNA target sequence that is 3 or more contiguous nucleotides. The claims are also drawn to an isolated polynucleotide encoding a modified plant zinc finger protein that further encodes a functional domain that is a repressive or activation domain. The claims are also drawn to an expression vector and a host cell.

Takatsuji et al. teach an isolated polynucleotide encoding a modified petunia plant zinc finger protein comprising a tandem array of two canonical C2H2 zinc fingers zinc fingers, said protein having one or more amino acids deleted between the zinc fingers (page 23370 Figure 2; page 23371 Figures 3-5; page 23372 Figures 6-7). The modified petunia plant zinc finger proteins taught by Takatsuji et al. bind to a DNA target sequence that is 3 or more contiguous nucleotides. The modified petunia plant zinc finger proteins taught by Takatsuji et al. further encode a functional maltose-binding protein domain that represses protein aggregation and degradation and activates protein solubility and stability. While Takatsuji et al. do not teach that their zinc fingers were obtained by rational design or selection, the polynucleotides taught by Takatsuji et al. necessarily anticipate the polynucleotides of claims 6-8, because the polynucleotides taught by Takatsuji et al. meet all the structural limitations of claim 5, from which claims 6-8 depend.

Claims 1-8, 10 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Coupland et al. (U.S. Patent No. 6,077,994 A, filed October 20, 1997 and issued June 20, 2000).

The claims are drawn to an isolated polynucleotide encoding a modified plant zinc finger protein comprising a tandem array of non-canonical zinc fingers, one or more of which is obtained by rational design or selection, wherein said protein binds to a DNA target sequence that is 3 or more contiguous nucleotides.

Coupland et al. teach an isolated polynucleotide encoding an *Arabidopsis* CONSTANS plant zinc finger protein comprising a tandem array of two non-canonical zinc fingers (columns 22-23 Example 3). The *Arabidopsis* CONSTANS plant zinc finger protein taught by Coupland et al. has the inherent ability to bind to a target DNA sequence that is 3 or more contiguous nucleotides. The *Arabidopsis* CONSTANS plant zinc finger protein taught by Coupland et al. is modified in that its coding sequence is operably linked to a heterologous promoter. While Coupland et al. do not teach that their zinc fingers were obtained by rational design or selection, the polynucleotides taught by Coupland et al. necessarily anticipate the polynucleotides of claims 6-8, because the polynucleotides taught by Coupland et al. meet all the structural limitations of claim 5, from which claims 6-8 depend.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
September 17, 2003

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600